

Attorney Docket No.: 960296.97290
Applicant(s): Attie/Gillian-Daniel/Bates
Application No.: 09/620,820 Filed: 07/21/2000
Group Art Unit: 1636
Office Action Dated: January 28, 2008
Amendment/Response dated July 28, 2008
Examiner: Celine X. Qian

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Currently Amended) A method for the lowering of serum cholesterol levels in a mammal comprising the steps of
~~making a genetic construct comprising (1) a protein coding sequence encoding for the expression of a fusion protein, the fusion protein including (a) a truncated form of a low density lipoprotein receptor, which includes the domain providing the function of binding to low density lipoprotein, but does not include the domain of the native protein associated with membrane binding or the domain associated with O-linked sugars, and (b) a localization domain, which directs localization of the fusion protein to the interior of a cell in the mammal so that the fusion protein will become localized to the endoplasmic reticulum, and (2) a promoter effective in the cells of the mammal to express the protein coding sequence; and~~
~~delivering the genetic construct into the vein of the mammal such that the expression and production of the fusion protein in the mammal results in the lowering of serum cholesterol in the mammal~~
preparing a nucleic acid construct comprising a DNA sequence encoding a fusion protein, operably linked to a promoter for expression in a cell, wherein the fusion protein comprises (a) a truncated soluble low density lipoprotein receptor, which includes the functional low density lipoprotein binding domain, but does not include the membrane binding domain or the domain associated with O-linked sugars, and (b) a localization domain signal peptide, which retains the fusion protein in the endoplasmic reticulum of a cell; and
administering the nucleic acid construct systematically to the mammal, wherein expression and production of said fusion protein results in the lowering of serum cholesterol levels in said mammal.

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2. (Currently Amended) A method as claimed in claim 1 wherein the low density lipoprotein receptor is ~~LDLR~~³⁵⁴ LDL-R.

3. (Original) A method as claimed in claim 1 wherein the localization domain is selected from the group consisting of the amino acid sequences KDEL, KEEL, HDEL, DDEL, QDEL, ADEL and SDEL.

4. (Original) A method as claimed in claim 1 wherein the localization domain is KDEL.

5.-8. (Cancelled)

9. (Currently Amended) ~~A DNA construct comprising a promoter operably linked to a protein coding sequence, the protein coding sequence coding for the expression of a fusion protein comprising (a) truncated form of a low density lipoprotein receptor, which includes the domain providing the function of binding to low density lipoprotein but does not include the domain of the native protein associated with membrane binding or the domain associated with O-linked sugars, and a localization domain signaling for the transport of the fusion protein to the endoplasmic reticulum of a cell, such that the construct is effective, when delivered into the vein of a mammal, to lower serum cholesterol in the mammal~~

A nucleic acid construct comprising a DNA sequence encoding a fusion protein, operably linked to a promoter for expression in a cell, wherein the fusion protein comprises
(a) a truncated soluble low density lipoprotein receptor, which includes the functional low density lipoprotein binding domain, but does not include the membrane binding domain or the domain associated with O-linked sugars, and

(b) a localization domain signal peptide, which retains the fusion protein in the endoplasmic reticulum of a cell.

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10. (Currently Amended) A DNA construct as claimed in claim 9 wherein the low density lipoprotein receptor is ~~LDLR~~³⁵⁴ LDL-R.

11. (Original) A DNA construct as claimed in claim 9 wherein the localization domain is selected from the group consisting of the amino acid sequences KDEL, KEEL, HDEL, DDEL, QDEL, ADEL and SDEL.

12. (Original) A DNA construct as claimed in claim 9 wherein the localization domain is KDEL.

13.-16. (Cancelled)

17. (Currently Amended) ~~A DNA construct comprising a promoter operably linked to a protein coding sequence, the protein coding sequence coding for the expression of a fusion protein, which includes the first 354 amino acids of the low density lipoprotein receptor fused to the amino acid sequence KDEL, such that the construct is effective, when delivered into the vein of a mammal, to lower serum cholesterol in the mammal~~

A nucleic acid construct for the lowering of serum cholesterol levels in a mammal comprising a DNA sequence encoding a fusion protein, operably linked to a promoter for expression in a cell, wherein the fusion protein comprises

(a) a truncated soluble low density lipoprotein receptor, LDL-R³⁵⁴, and

(b) a localization domain signal peptide, KDEL, which retains the fusion protein in the endoplasmic reticulum of a cell.

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18. (New) A nucleic acid construct for the lowering of serum cholesterol levels in a mammal comprising a DNA sequence encoding a fusion protein, operably linked to a promoter for expression in a cell, wherein the fusion protein comprises

- (a) a truncated soluble low density lipoprotein receptor, LDL-R³⁵⁴, and
- (b) a localization domain signal peptide, which retains the fusion protein in the endoplasmic reticulum of a cell, wherein the localization domain is selected from the group consisting of the amino acid sequences KDEL, KEEL, HDEL, DDEL, QDEL, ADEL and SDEL.

19. (New) A method for the lowering of serum cholesterol levels in a mammal comprising the steps of:

preparing a nucleic acid construct comprising a DNA sequence encoding a fusion protein, operably linked to a promoter for expression in a cell, wherein the fusion protein comprises

- (a) a truncated soluble low density lipoprotein receptor, LDL-R³⁵⁴, and
- (b) a localization domain signal peptide, KDEL, which retains the fusion protein in the endoplasmic reticulum of a cell; and

administering the nucleic acid construct systematically to the mammal, wherein expression and production of said fusion protein results in the lowering of serum cholesterol levels in said mammal.

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20. (New) A method for the lowering of serum cholesterol levels in a mammal comprising the steps of:

preparing a nucleic acid construct comprising a DNA sequence encoding a fusion protein, operably linked to a promoter for expression in a cell, wherein the fusion protein comprises

(a) a truncated soluble-low density lipoprotein receptor, LDL-R³⁵⁴, and

(b) a localization domain signal peptide, which retains the fusion protein in the endoplasmic reticulum of a cell, wherein the localization domain is selected from the group consisting of the amino acid sequences KDEL, KEEL, HDEL, DDEL, QDEL, ADEL and SDEL; and

administering the nucleic acid construct systematically to the mammal, wherein expression and production of said fusion protein results in the lowering of serum cholesterol levels in said mammal.